----------Chapter 11 *(Chapter 8)*- Molecular Genetics IV ----------

(each task is dedicated by page number and task number in 2009 edition book, or in 2005 edition book)

p. 118, Task 1a (p.125, T1): II/3 is not a carrier, II/4 and II/5 are carriers

Task 1b: the fetus III/1 does not carry mutant allele

p. 120, Task 2-1 (p.127, T2-1): We cannot (it is impossible to) determine which members of the 3rd generation inherited (are carriers of) a mutated allele.

p. 121, Task 2-2 (p.127, T2-2): After additional genotyping of I/2, we can determine III/1 and III/3 as non-carriers of mutant allele and III/2 as a carrier of mutant allele; but, for III/4 and III/5, it is (still) impossible to determine their genotypes.

Task 2-3 (p.127, T2-3): By direct diagnostics of the mutation, males III/1 and III/3 are proven as unaffected and III/2 as a carrier; newly, III/4 is determined as unaffected and III/5 as a carrier of a causal (mutant) allele.

Advantage of direct diagnostics of a deleterious allele: the diagnosis is fully informative even in family with incomplete data.

p. 123, Task 3a: *In the Fig. No. 11/6b there is mistake in described length of the fragments. Correctly, there should be: (from top to bottom) 353bp, 329bp, 263bp and 248bp!*

The number of CAG repeats (genotype) is 20/42 in I/1, 15/20 in I/2, 15/50 (expansion) in II/1, 20/42 in II/2, 15/15 in II/3, and 20/20 in II/4; and in the third generation, it is 15/20 in III/1, 15/15 in III/2, and 15/42 in III/3.

Task 3b: Risk of manifestation of HD - penetrance is full, those who inherit the mutant allele eventually develop the disease. In this family there is III/3 affected, eventually he will develop clinical signs of Hungtington disease.

N.B.: 36–39 repeats result in a reduced-penetrance, with a much later onset and slower progression of symptoms; in some cases the symptoms are never noticed. With very large repeat counts (in about 7% of HD carriers), HD can occur under the age of 20, when it is then referred to as juvenile HD.

p. 125, Task 4-1 (p.130, T4-1): In this family, FAP is linked to allele 10 of intragenic (CA)n polymorphism. In the 3rd generation, only III/2 is proven as a carrier of the mutant allele. Individuals III/4 and III/5 could not be proven – in this part of family the analysis has been uninformative (because II/4 is homozygous for allele 10).

Task 4-2 (p.131, T4-2): Suggestion – i) analyze another polymorphism, in which the II/4 is heterozygous or ii) use direct diagnostics with direct detection of mutation(s) in APC gene.

p. 126, Task 5:

Family	An extra chromosome 21 inherited from:	The non-disjunction occurred in meiotic division:
1	mother or father	I
2	mother	I
3	mother	II

p. 127, Task 6: Suspect No. 1 matches the specimen.